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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/448,420	11/22/1999	MICHAEL SEUL	000973/0003	5017

7590 04/09/2002  
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EXAMINER

PONNALURI, PADMASHRI

ART UNIT	PAPER NUMBER
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1627

DATE MAILED: 04/09/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.  
**09/448,420**

Applicant(s)

**Seul et al**

Examiner  
**Padmashri Ponnaluri**

Art Unit  
**1627**



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on Mar 4, 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 129-159 is/are pending in the application.
- 4a) Of the above, claim(s) 152 and 153 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 129-151 and 154-159 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some\* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

### Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 17, 18
- 18) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

Art Unit: 1627

### DETAILED ACTION

1. The request filed on 1/23/02 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/448,420 is acceptable and a CPA has been established. An action on the CPA follows.
2. The preliminary amendment E, filed on 3/4/02 has been considered and entered into the application.
3. Claims 98-128 have been canceled and new claims 129-159 have been added by the amendment E, filed on 3/4/02.
4. Claims 129-159 are currently pending in this application.
5. Claims drawn to the invention of group I, and species nucleotide (for compounds), binding to a probe (for property) and static planar array (for array) were elected without traverse on 10/11/00 for prosecution in this application. And applicants have confirmed the election in response filed on 5/10/00. The instant claims 129-159 are drawn to the elected group of invention. However claims 152-153 are drawn to non-elected species.
6. Claims 152-153 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected species election. Election was made **without** traverse in Paper No. 10.
7. Claims 129-151 and 154-159 are currently being examined in this application.
8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1627

9. Claims 129-151, 154-159 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 129 recites in step (a), 'dividing a population of solid supports **into M batches....**' it is indefinite by reciting that the supports are divided into M batches without defining M. The claim no where ~~the claim~~ recites what is integer that represents M. Does applicants mean M has no specific defined number, which has no support in the specification. Applicants are requested to amend the claim.

Claim 129 is vague and indefinite by reciting 'decoding the fluorophore tag associated with the compound...', clarification is requested whether the tag is associated with the compound or the solid support.

Claim 129 is indefinite by reciting that in step (g) '.....decoding the fluorophore tag associated with the compound having property of interest to identify said compound.....' The claim recites in step (f) the library of compounds are contacted with a target biomolecule; and in step (g) decoding the fluorophore tag associated with the compound having the property of interest..... It is not clear how a compound of interest is separated or identified from the library of compounds, so that the fluorophore is decoded. From a library of compounds which are attached to solid supports and fluorescent tags are contacted with the target of interest, how is the

Art Unit: 1627

specific compound which binds to the target is identified, such that the tag associated with the compound is decoded. The claim later recites, '.... optically interrogating the fluorophore tag bound to the solid support on which the compound having the property of interest was produced.' It seems to be the claim is missing some other essential element, such that the fluorophore on the solid support on which the compound of interest is detected optically. It seems that the target biomolecule has another tag associated with it. Applicants are requested to clarify.

Claim 134 recites the limitation "the fluorophore tags" . There is insufficient antecedent basis for this limitation in the claim. Note that Claim 129 recites "fluorophore tags".

Claim 135 recites the limitation "the fluorophore tags" . There is insufficient antecedent basis for this limitation in the claim. Note that claim 129 recites 'fluorophore tag.'

Claim 136 recites the limitation "the fluorophore tags" . There is insufficient antecedent basis for this limitation in the claim. Note that Claim 129 recites "fluorophore tag".

Claim 137 recites the limitation "the fluorophore tags" . There is insufficient antecedent basis for this limitation in the claim. Note that Claim 129 recites "fluorophore tag".

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who

Art Unit: 1627

has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

11. Claims 129-138, 142-146, 151, 154 and 159 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 93/06121 (Dower et al).

Dower et al disclose a general stochastic method for synthesizing random oligomers which can be used to synthesize compounds to screen for desired properties. The reference discloses that the use of the identification tags on the oligomers facilitate identification of oligomers with desired properties (see the abstract). The reference discloses that the random oligomers are synthesized on solid supports, or particles, but many be cleaved from these supports to provide a soluble library. The oligomers are composed of a sequence of monomers, and the library is screened to isolate individual oligomers that bind to a receptor, or possess a desired property (see page 4). The reference discloses that an identifier tag is used to identify the sequence of monomers in the oligomer. The reference discloses that the identifier tag is directly attached to the oligomer with or without an accompanying particle, to the solid support upon which the oligomer is synthesized (see page 4). The reference discloses that the identifier tag may be composed of a set of light addressable compounds, such as fluorescent or phosphorescent compounds, which are incorporated into the beads or particles on which the oligomers of the oligomer library are synthesized. The reference discloses that the coded identifier tags may be used to so that each monomer is assigned a specific binary number (i.e., see page 26, lines 3-4) (refers to bits of binary code of the instant claims). The reference discloses such compounds are well known in the art (i.e., see last paragraph in page 4 bridging page 5). The reference discloses

Art Unit: 1627

a method for producing tagged synthetic oligomer libraries (i.e., see pages 15-19). The reference discloses split-pool synthesis of the oligomer library (i.e., see page 16). The reference discloses the method for identification of the sequence of the oligomer (i.e., page 19). The reference discloses that the tags may be attached immediately before, during , or after the monomer addition, as convenient as compatible with the type of identifier tag, modes of attachment and chemistry of oligomer synthesis. The identifier tag is added when the solid support that have undergone a specific monomer addition step are physically together so can be tagged as a group. The reference discloses that the fluorescent beads are recovered from the positive wells . The beads are removed and sorted by FACS. The reference discloses that the compounds of the library are identified using a competitive assay, in which diminished fluorescence caused by the oligomer library competing with the ligand are identified (i.e., see page 31). The reference clearly anticipates the claimed invention.

12. Claims 129-138, , 142-146, 151, 155-159 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 5,968,736 (Still et al) .

Still et al disclose methods for recording the reaction history of a solid support. The reference discloses encoded combinatorial chemistry, in which sequential synthetic schemes are recorded using organic molecules, which define choice of reactant, and stage, as the same or different bit of information. The reference discloses that various products can be produced in multistage synthesis, such as oligomers and synthetic non-repetitive organic molecules (see abstract). The reference discloses that nested families of compounds can be employed as

Art Unit: 1627

identifiers, where the number and/or position of a substituent define the choice, and alternatively detectable functionalities such as radioisotopes, fluorescers, halogens can be used (see abstract). The reference discloses that the invention provides methods and compositions for encoded combinatorial synthesis whereby at each stage of the synthesis one or more identifiers are provided which encode an event associated with a particle stage in the synthesis of the compound on the support (i.e., see column 7, lines 1-4). The reference discloses that the N identifiers, and M distinguishable states are provided (see column 7, lines 14-15); and in case if M is 2 where the two states could be the presence or absence of identifier, the synthesis thus defined by a base 2 or binary code (i.e., see column 7, lines 15-18) (refers to the fluorophore tag represents a bit of binary code of the instant claims). The reference discloses that the synthesis of oligomers on solid support begin with a number of beads, which would be divided into groups, and then add the reagents and the identifiers which encode the reagent and the stage of the reaction. And after the synthesis is completed, the compounds are screened for desired property either after detachment of the ligand (compound) from the bead or **while still attached** (i.e., see column 17, lines 4-6). The reference discloses that the beads with ligand attached are incubated in aqueous buffer with monoclonal antibody (for the property to be tested), and the fluorescent beads with attached monoclonal antibody are identified and separated by manually or using FACS from the unstained beads, so long as the tags are retained on the bead under the conditions of sorting. The reference teaches that the fluorescent beads with attached compound are identified from the unstained beads, thus, the reference analyzed the fluorescent data of the

Art Unit: 1627

beads, to identify the compound of interest in the library. Thus, the reference clearly anticipates the claimed invention.

13. Claims 129-159 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dower (WO 93/06121) in view of Metzeker et al (US patent 5,728,529).

Dower et al have been discussed supra.

The claimed invention differs from the prior art teachings by reciting that the fluorescent tags of specific chemical structures. Dower et al teach methods of synthesizing diverse collections of oligomers. Dower et al teach the use of identifier tags. Dower et al fail to teach the fluorescent tags of the specific structures of the claims 139-141. However, Metzeker et al teach alternative dye-labeled RNA, DNA for DNA analysis. The reference teaches a new class of dyes which have improved spectral characteristics and improved stability. The reference teaches that because of the improved properties of these dyes, they are useful in any method of detection of DNA, and the spectral properties of the fluorophores are similar in wavelength and intensity to be used with conventional equipment known in the art. Thus, it would have been obvious to a person skilled in the art at the time the invention was made to use the fluorescent dyes taught by Metzeker et al in the method of oligomer library synthesis and identification of the compounds of interest using identifier tags taught by Dower et al, because Metzeker et al teach novel class of fluorescent dyes which can be useful to label the DNA, RNA, and has improved spectral properties, and can be use din any assay method, and Dower et al teach a method of using identifier tags (fluorescent or oligonucleotide) to label the solid supports to which an oligomer of

Art Unit: 1627

a oligomer library is attached. A person skilled in the art at the time the invention was made to use the fluorescent dyes taught by Metzeker et al in the method of combinatorial library of compound synthesis with the expectation of identifying the compound of interest using conventional equipment known in the art.

14. Applicant's arguments filed on 3/4/02 , regarding the art rejection of claims over Dower et al have been fully considered but they are not persuasive.

Applicants argue that Dower does not anticipate the claim, because Dower does not disclose decoding the tag without physically isolating the solid support of interest from other solid supports. Applicants arguments have been considered but are not persuasive. Because the previous office action in paragraph 19 states that "*Dower et al teach method for screening synthetic oligomer libraries with receptors (see page 29). The reference teaches that the oligomer library can be synthesized on microscopic beads with identifier tag encoding the oligomer sequence, the microscopic beads are placed in individual compartments, and the oligomers are cleaved from the beads and remain contained in the compartment along with the bead and the attached identifier tags. The bottom surface is coated with receptor (refers to new claims 123-125) (see page 30). So the beads of interest are not separated from the mixture to accomplish the identification.*"

Applicants further argue that dower does not teach binary code. Applicants arguments are not persuasive, because Dower in page 26 teaches that the coded identifier tags may be used to so that each monomer is assigned a specific binary number.

Art Unit: 1627

15. Applicant's arguments filed on 3/4/02, regarding the rejection of claims over Still et al have been fully considered but they are not persuasive.

*Applicants argue that Still does not teach or suggest that the identification of the compounds of interest may be carried out without removing the beads from the mixture and without cleaving the identifier tag from the beads for further analysis. Applicants arguments have been considered but are not persuasive, because Still et al teach in column 17, after the synthesis of product is complete, they are screened for a desired property either after detachment of the ligand from the bead or while still attached.*

16. Applicant's arguments filed on 3/4/02 regarding the rejection of claims over Dower and Metzeker et al have been fully considered but they are not persuasive. Applicants arguments have been considered but are not persuasive, for the reasons discussed supra.

17. No claims are allowed.

18. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to P. Ponnaluri whose telephone number is (703) 305-3884. The examiner

Art Unit: 1627

can normally be reached on Monday to Thursday from 6.30 AM to 4.00 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat, Ph.D., can be reached on (703) 308-2439. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

P. Ponnaluri  
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Art Unit 1627  
05 April 2002

  
PADMASHRI PONNALURI  
PRIMARY EXAMINER